CSBC Investigator Highlight

Dr. Darryl Shibata is Investigating the Evolution of Cancer at Multiple Scales

Darryl Shibata, M.D., is a CSBC investigator at the University of Southern California (USC) who uses evolutionary models to advance cancer systems biology. According to him, "the principles of evolution fit naturally into systems biology, since biology is basically built by evolution."

In this interview, he discusses mentors who helped him during his career journey, his views on cancer systems biology, and his CSBC research investigating the evolution of cancer.

- **Who inspired you during your career journey?**

  While I was a resident in pathology, the polymerase chain reaction (PCR) became a new tool for research. Around this time, a professor named Norman Arnheim moved to USC from the Cetus Corporation, where PCR was invented. I thought PCR was such a neat technology, so I wandered down the hall to meet him. I asked, "Can I volunteer to work in your lab?" and he let me start doing experiments. He was inspirational and supportive.

  There's also Simon Tavaré, a mathematician who worked at USC. About 20 years ago, I made a big effort to become more quantitative in my research, because biology is pretty descriptive. Simon is a talented mathematician and a very personable guy who helped me in this effort. He's easy to talk to and helped me learn about systems biology approaches.

- **From your clinical perspective, why are systems biology approaches important for cancer research?**

  In cancer research, we measure lots of stuff. We have all this data and it's pretty hard to integrate it into a more coherent picture. It seems like systems biology approaches are inherently a way of integrating a lot of information into a coherent picture.

- **What advice do you give to trainees who want to study cancer systems biology?**

  They should always look at the bigger picture. Even if they are working on a very specific project, they should try and look at a bigger picture and see how their work could be integrated into a bigger picture.

- **Can you describe your CSBC research?**

  What we're trying to do with this project is to use principles of evolution to describe cancer biology.

  One of the things I'm very interested in using for our project is the coalescent theory, which is a mathematical framework that says if you go back in the past, then all cells or all people will eventually coalesce to a single individual. It's guaranteed to work, according to the mathematicians, and it's always good when you have guarantees in biology. Currently, I'm trying to take a tumor that shows up in a person and then reconstruct the history of that tumor using the coalescent theory.

In medicine, the basis of a diagnosis is a history and a physical. You get the history from the patient and then you do a physical where you test to see what's there. Oftentimes, a medical trainee, like a medical student or a new resident, will do a lot of testing and won't really know what to make of all the test results. A more experienced doctor will take a really good history. S/he'll ask, "When did this start? How do you feel? What happened?" With this information, the doctor knows what tests to order to confirm what the history is telling him/her and knows what the results of the tests mean.

With our project focused on evolution, we're looking back to try and see the history of the tumor. The idea is that nothing in biology makes sense except by the light of evolution. In other words, if you understand the history of the tumor, then you may better understand what it is you're measuring.

- **How will understanding the evolution of cancer ultimately help cancer patients?**

When someone has cancer, it's the product of evolution. When we try to cure patients with cancer, we need to use evolutionary principles. If you want to cause a species (or tumor) to thrive or become extinct, you need to evolutionarily know what to do.

Even when cancers don't have a currently known cure, you can still manipulate the evolution. This is the idea of adaptive therapy, where you treat a tumor in different ways over time based on its predicted responses. It's like playing a game of chess. You learn as you play the game and decide your next move based on how you predict your opponent will respond. The goal of adaptive therapy is to control the disease and help the patient live longer with a high quality of life.